

REMARKSRejection of Claims 1-23 and 30-38 Under 35 U.S.C. § 103(a)

Claims 1-23 and 30-38 are rejected under 35 U.S.C. § 103(a) as being obvious over McGall, *et al.* (U.S. Patent No. 5,412,087; hereinafter “the ‘087 Patent”) in view of McGall, *et al.* (WO 98/39348; hereinafter “the ‘348 Publication”).

*Summary of the Rejection*

The Examiner states, apparently referring to the ‘087 Patent, that this patent teaches methods and compositions of matter for immobilizing biological polymers on the surface of a solid support. The Examiner states that the ‘087 Patent discloses a number of nitrobenzylic photoprotecting groups, namely 6-nitroveratryloxycarbonyl, 6-nitropiperonyloxycarbonyl,  $\alpha,\alpha$ -dimethyldimethoxybenzyloxycarbonyl, methyl 6-nitroveratryloxycarbonyl, methyl-6-nitropiperonyloxycarbonyl and 1-pyrenylmethyl. The Examiner states that the ‘087 Patent does not disclose the specific photolabile protecting groups recited in the instant claims.

The Examiner summarizes the ‘348 Publication as teaching photocleavable groups having the general formula Ar-C(R1)(R2)-O-C(O)-, where Ar is an optionally substituted fused polycyclic aryl group. The Examiner notes that one possible Ar is a naphthyl group and that one possible substituent is a nitro group. The Examiner states that the photocleavable groups can be attached to a monomeric building block.

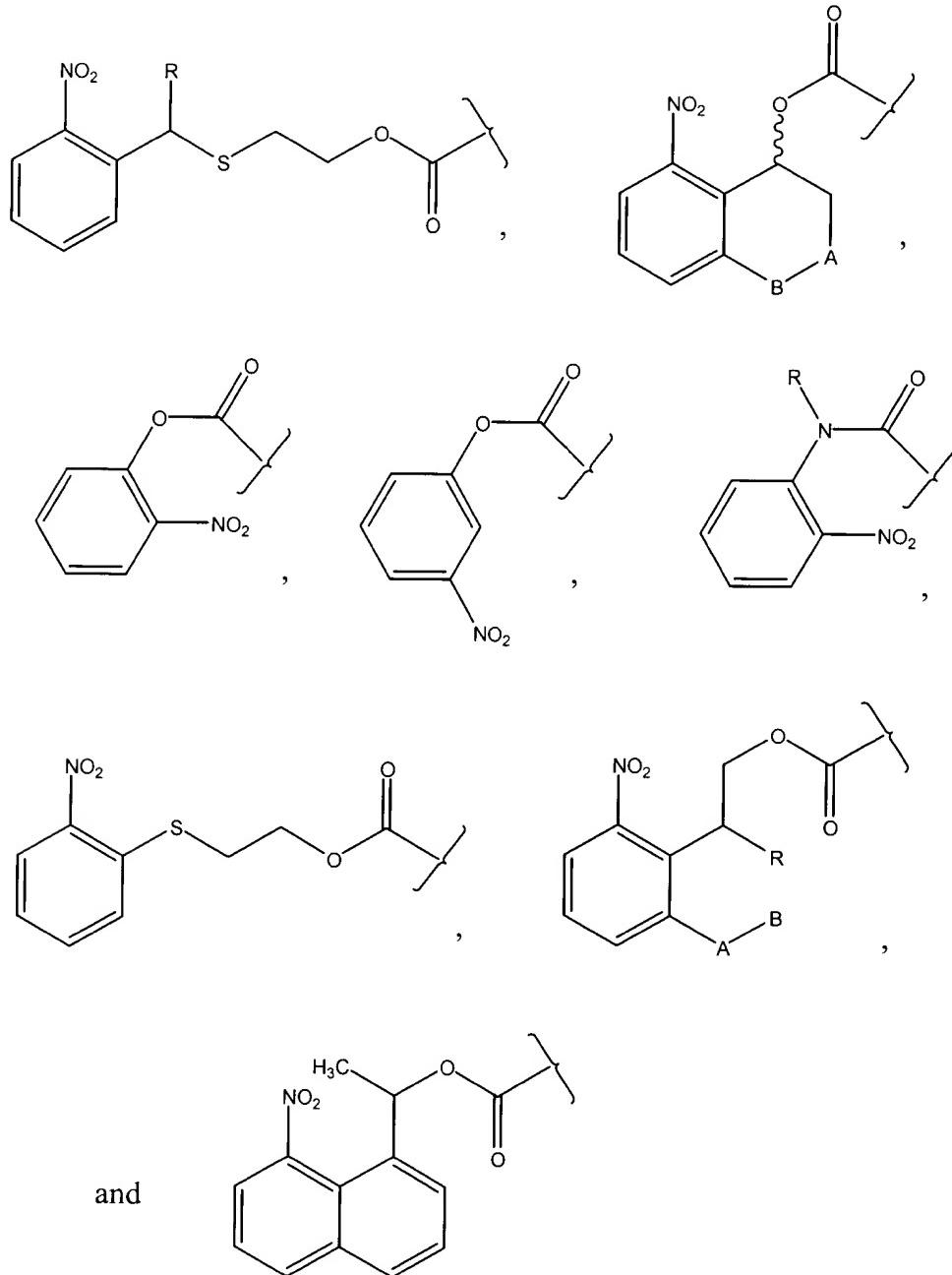
The Examiner concludes that it would have been obvious to modify the teachings of the ‘087 Patent with the teachings of the ‘348 Publication to make the compounds of the present invention and to use these compounds in attaching a molecule to a solid support. For the non-polycyclic (e.g., benzylic) groups, the Examiner states that it would have been obvious to modify the teachings of the ‘087 Patent and that one would have been motivated to substitute one nitrobenzylic group for another.

*Restriction Requirement*

A continuation-in-part of the present application, Application No. 09/950,982, was filed September 11, 2001 (hereinafter referred to as “the CIP application”) and is being examined by the Examiner handling the present application. A Restriction Requirement for the CIP application was mailed March 31, 2003. In that Restriction Requirement, the claims were

divided into three groups based on the Examiner's assertion that the compounds of Groups I-III are chemically and structurally distinct.

Claim 1, which is in Group I, is directed to a compound represented by the structural formula Y-X, where X is a leaving group or a compound having a masked reactive site and Y is a photolabile protecting group selected from the group consisting of:



wherein:

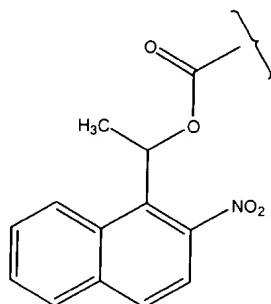
R is -H, an optionally substituted alkyl, or an optionally substituted aryl;

A is -O-, -S-, -NR-, or -(CH<sub>2</sub>)<sub>k</sub>-;

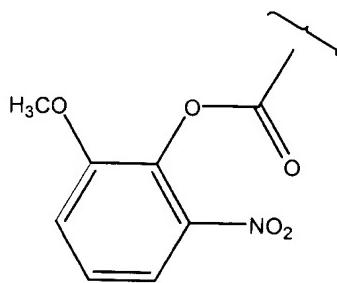
k is 0 or an integer from one to about three; and

B is a monovalent or divalent aprotic weakly basic group.

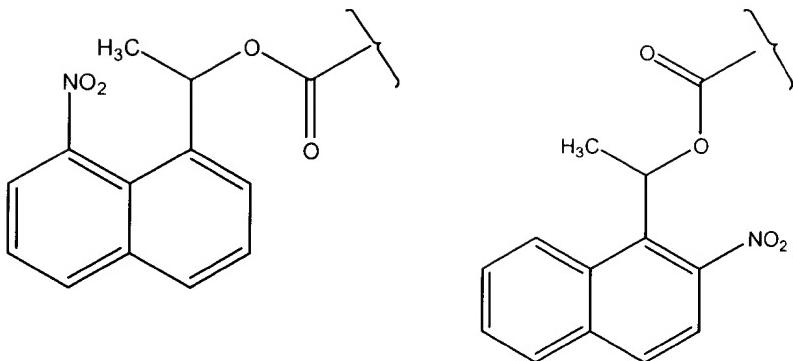
Claim 39, which is part of Group II, is directed to a compound represented by the structural formula Y-X, where X is a leaving group or a compound having a masked reactive site and Y is a photocleavable protecting group. One of the recited photocleavable protecting groups is represented by the formula:



Claim 50, which is part of Group III, is directed to a compound represented by the structural formula Y-X, where X is a leaving group or a compound having a masked reactive site and Y is a photolabile protecting group. One of the recited photolabile protecting groups is represented by the formula:

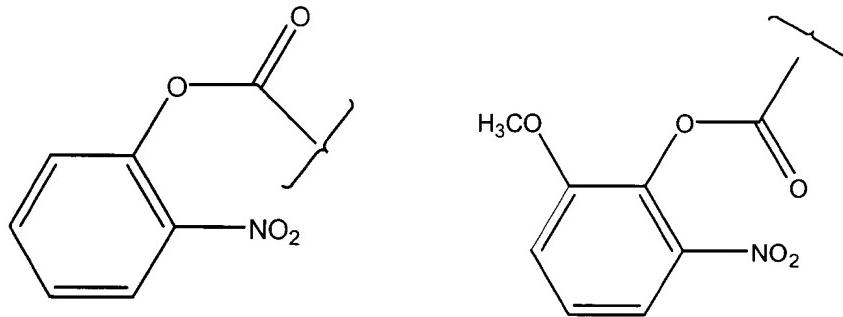


The photocleavable protecting group of Claim 39 (Group II) that is shown above differs from the last photocleavable protecting group recited in Claim 1 (Group I) only in the position of the nitro group. The two protecting groups are shown again for comparison:



The nitro group is at the 8-position of the naphthyl group in Claim 1, while the nitro group is at the 2-position of the naphthyl group in Claim 39. Because X is defined identically in Claims 1 and 39, compounds encompassed by Claims 1 and 39 (Groups I and II) that the Examiner has deemed patentably distinct in the CIP application differ only by the position of the nitro group on the naphthyl group.

The photocleavable protecting group of Claim 50 (Group III) that is shown above differs from the third photocleavable protecting group recited in Claim I (Group I) only by the addition of a methoxy substituent. The two protecting groups are shown again for comparison:



In the protecting group of Claim 50, the methoxy group is located at the 6-position of the phenyl ring (fixing the nitro group at the 2-position for consistency with the protecting group of Claim 1). Because X is defined identically in Claims 1 and 50, compounds encompassed by Claims 1 and 50 (Groups I and III) that the Examiner has deemed patentably distinct in the CIP application differ only by an additional substituent on the phenyl ring.

According to MPEP § 803, an application can properly be “required to be restricted to one of two or more claimed inventions only if they are able to support separate patents...”. Therefore, the structural differences between the photocleavable protecting groups discussed

above can be used to guide an assessment of patentably distinct protecting groups. This test is applied below to compare the structural differences between protecting groups (and the compounds they protect) deemed patentably distinct in the CIP application with the structural differences between claimed protecting groups in the instant application and prior art protecting groups.

The instant rejection is not consistent with the Restriction Requirement made in the CIP application of the present application. Many of the protecting groups considered to be patentably distinct in the Restriction Requirement have fewer structural distinctions as compared with the recited protecting groups than the prior art protecting groups upon which the obviousness rejection is based, as discussed in detail below.

*Instant Claims Are Patentably Distinct From The Prior Art*

The test described above is appropriately applied to the instant claims, because instant Claim 1 is encompassed within Claim 1 of the CIP application. Specifically, the subject matter of Claim 1 in the present application and Claim 1 in the CIP application relate to similar subject matter differing in scope. Claim 1 of the present application is directed to a compound represented by the formula M-Y, where M is a monomeric building block, a solid surface or gel having a reactive site that is masked by Y, and Y is a photolabile protecting group. Claim 1 of the CIP application is directed to a compound represented by the structural formula Y-X, where X is a leaving group or a compound having a masked reactive site and Y is a photolabile protecting group. The photolabile protecting groups in Claim 1 of the present application are all recited in Claim 1 of the CIP application (the CIP application recites additional protecting groups). Thus, Claim 1 of the CIP application completely encompasses Claim 1 of the present application and ***what is patentably distinct from Claim 1 of the CIP application is also patentably distinct from Claim 1 of the instant application.*** Claims 5-23 and 30-38 of the present application recite 2 or 3 additional photolabile/photocleavable protecting groups as compared to Claim 1; however, these additional protecting groups are all recited in Claim 1 of the CIP application.

Naphthyl Protecting Groups

The ‘348 Publication discloses protecting groups having the formula:

Ar-C(R<sub>1</sub>)(R<sub>2</sub>)-O-C(O)-, where Ar is an optionally substituted fused polycyclic aryl or heteroaromatic group or a vinylogous derivative thereof and R<sub>1</sub> and R<sub>2</sub> are independently -H or optionally substituted alkyl, alkenyl, alkynyl, aryl, heteroaromatic groups.

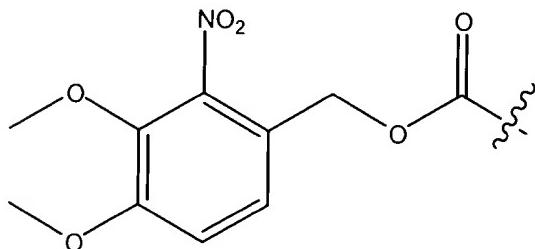
The ‘087 Patent does not teach protecting groups with fused polycyclic groups; therefore, the teachings of the ‘087 Patent cannot be combined with the teachings of the ‘348 Publication with regard to the structures of these protecting groups.

In the Restriction Requirement discussed above, the Examiner deemed an alpha-methyl-2-nitronaphthylmethoxycarbonyl group to be patentably distinct from an alpha-methyl-8-nitronaphthylmethoxycarbonyl group. Thus, it appears that the position of the nitro group on a naphthyl ring is a patentably distinct feature.

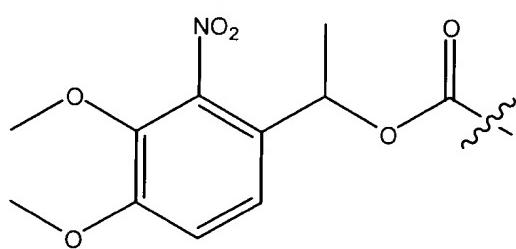
Although the ‘348 Publication discloses that naphthyl is a suitable value of Ar and that an Ar group can be substituted with, *inter alia*, a nitro group, there is no disclosure of a nitro-substituted naphthyl moiety in the ‘348 Publication. As such, the ‘348 Publication does not disclose the positions on a naphthyl group that can be substituted with a nitro group to produce a photolabile protecting group. Thus, using the standard applied in the Restriction Requirement, the naphthyl protecting group recited in the instant claims is patentably distinct from the optionally substituted fused polycyclic protecting groups disclosed by the ‘348 Publication.

“Nitrobenzylic” Protecting Groups

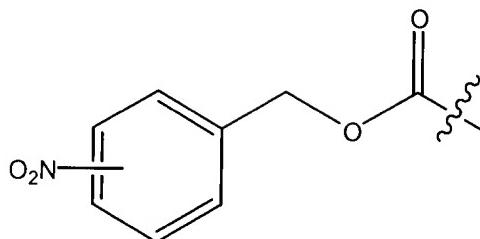
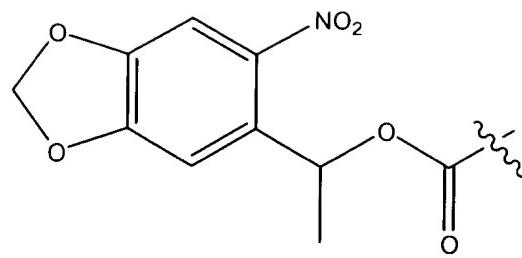
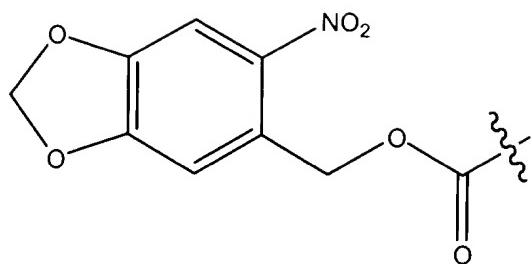
The ‘087 Patent teaches five nitrobenzylic photolabile protecting groups at column 8, lines 24-50. The five nitrobenzylic protecting groups are shown below:



NVOC



MeNVOC

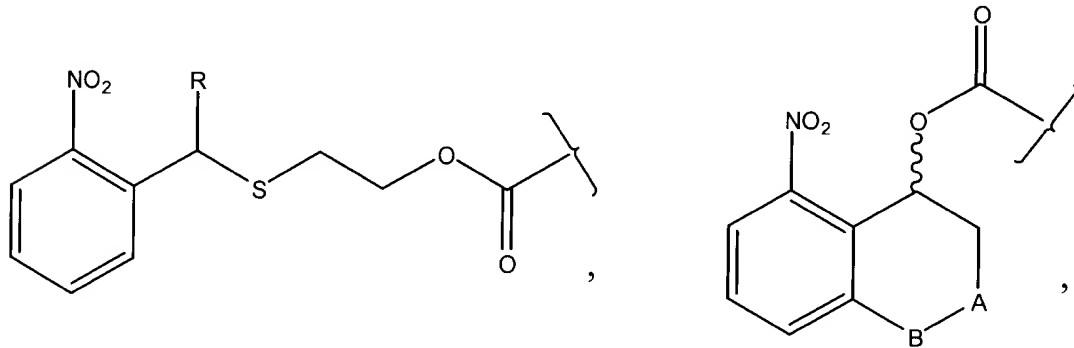


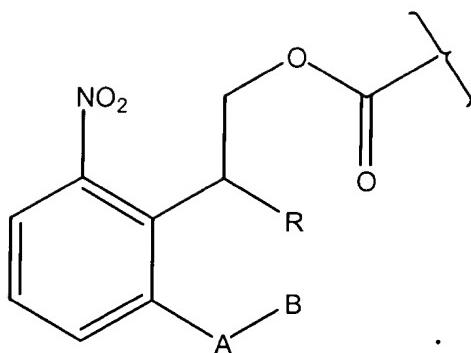
NBOC

(Note that pyrenylmethyl is not a nitrobenzylic group, contrary to the Examiner's statement.)

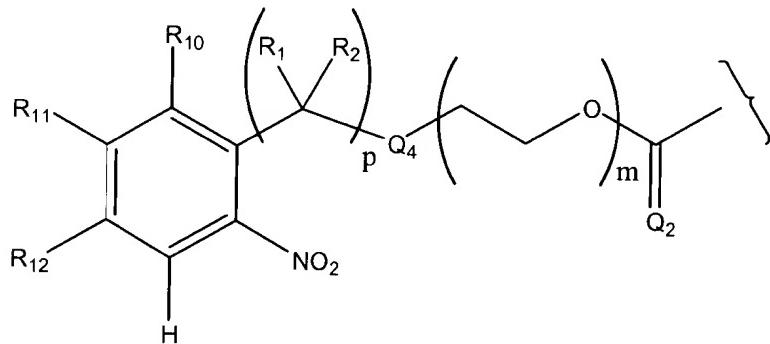
The '348 Publication does not teach nitrobenzylic protecting groups; therefore, the '348 Publication cannot be combined with the '087 Patent with respect to the structures of nitrobenzylic protecting groups.

Three protecting groups having a nitrobenzyl moiety are recited in the claims of the present application, as shown below:

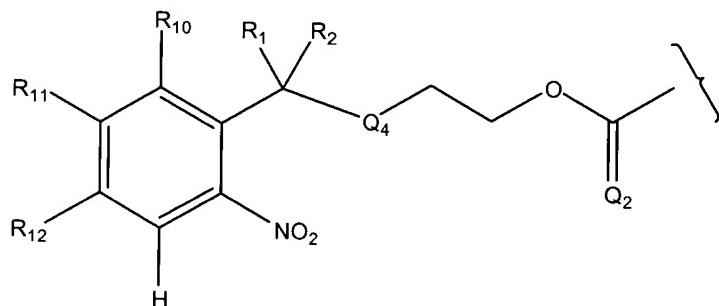




In the Restriction Requirement discussed above, these three protecting groups were deemed to be patentably distinct from a protecting group having the following generic structure:



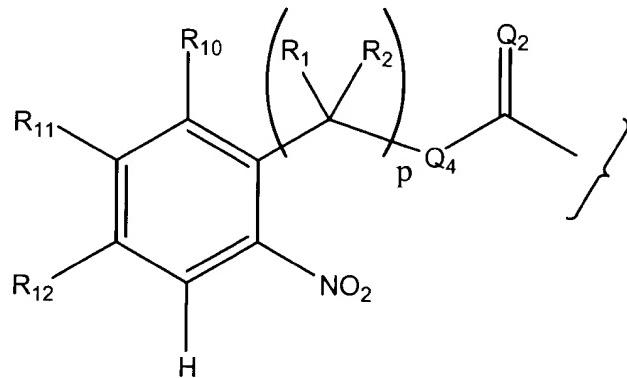
In Claim 51 of the CIP application, m and p are both 1, resulting in the following structure:



The protecting groups of Claim 51 differ from the first of the three protecting groups shown above in that R<sub>1</sub>, R<sub>2</sub>, R<sub>10</sub>, R<sub>11</sub>, R<sub>12</sub>, Q<sub>2</sub> and Q<sub>4</sub> are not specified in the generic structure. Nevertheless, the values of R<sub>1</sub>, R<sub>2</sub>, R<sub>10</sub>, R<sub>11</sub>, R<sub>12</sub>, Q<sub>2</sub> and Q<sub>4</sub> can be selected to arrive at the structure of the first of the three protecting groups shown above. In contrast, the nitrobenzylic compounds disclosed in the '087 Patent do not have the thioethylene group between the nitrobenzyl moiety and the oxycarbonyl moiety. Thus, there are fewer structural differences between protecting groups that have been deemed patentably distinct in the CIP application than

between the instantly claimed protecting group and the protecting groups disclosed in the '087 Patent. Therefore, the first of the three protecting groups shown above is clearly patentably distinct over the '087 Patent.

In Claim 53 of the CIP application, m is 0 and p is 1 or 2, resulting in the following structure:

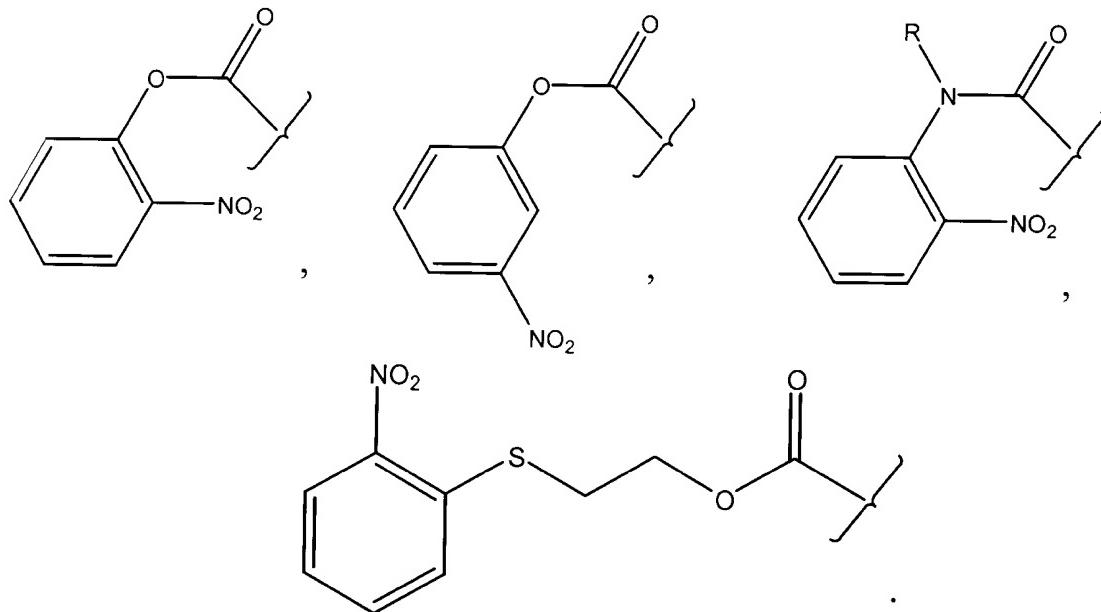


The protecting groups of Claim 53 of the CIP application share the same structural backbone as the second and third of the three protecting groups shown above. In contrast, the nitrobenzylic compounds disclosed in the '087 Patent do not have either (i) two methylenes between the nitrobenzyl moiety and the oxycarbonyl moiety or (ii) a ring that includes R<sub>10</sub>, one of R<sub>1</sub> and R<sub>2</sub> and the carbon atoms to which they are attached. Thus, there are fewer structural differences between protecting groups that have been deemed patentably distinct in the CIP application than between the instantly claimed protecting groups and the protecting groups disclosed in the '087 Patent. Therefore, the second and third of the three protecting groups shown above are clearly patentably distinct over the '087 Patent.

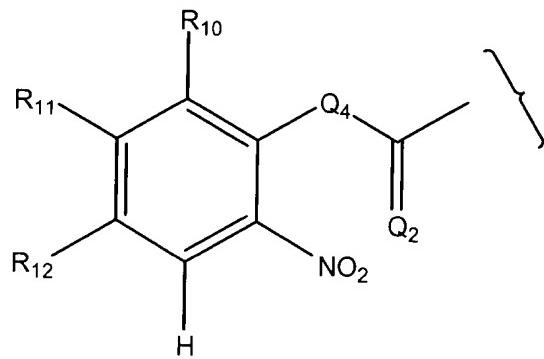
Furthermore, each of these three groups is structurally distinct from the protecting groups disclosed in the '087 Patent. The first group has a thioethylene linkage between the nitrobenzyl moiety and the oxycarbonyl group; the '087 Patent does not teach or otherwise suggest nitrobenzylic protecting groups having a thioethylene linkage. The second protecting group includes a -CH<sub>2</sub>-A-B- moiety that connects the 6-position of the benzene ring (nitro group is at the 2-position) and the benzylic methylene group to form a cyclic group fused to the benzyl moiety. The '087 Patent does not teach or otherwise suggest benzylic groups with a fused cyclic group that incorporates the benzylic methylene group. The third protecting group differs from

the protecting groups disclosed in the '087 Patent in that there is an extra methylene group between the benzylic methylene group and the oxycarbonyl group, as well as in that -B is an aprotic, weakly basic group meta to the nitro group and ortho to the benzylic methylene group. The '087 Patent does not teach or otherwise suggest modifying a nitrobenzyl protecting group to include these structural features.

The Examiner has apparently also included the following four protecting groups in the category of nitrobenzylic protecting groups, although none of these groups has a nitrobenzyl moiety. The four protecting groups are as follows:



In the Restriction Requirement discussed above, these four protecting groups were deemed to be patentably distinct from the protecting group recited in Claim 49 of the CIP application, the structure of which is as follows:



The protecting groups of Claim 49 differ from the first three of the four protecting groups shown above in that  $R_{10}$ ,  $R_{11}$ ,  $R_{12}$ ,  $Q_2$  and  $Q_4$  are not specified in the generic structure. Nevertheless, the values of  $R_{10}$ ,  $R_{11}$ ,  $R_{12}$ ,  $Q_2$  and  $Q_4$  can be selected to arrive at the structure of the first of the three protecting groups shown above. In contrast, the nitrobenzylic compounds disclosed in the '087 Patent do not have a direct bond between the nitrobenzyl moiety and the oxycarbonyl or aminocarbonyl moiety. Thus, there are fewer structural differences between protecting groups that have been deemed patentably distinct in the CIP application than between the instantly claimed protecting group and the protecting groups disclosed in the '087 Patent. Therefore, the first three of the four protecting groups shown above are clearly patentably distinct over the '087 Patent.

Moreover, it is clear that each of the four claimed protecting groups differs from the disclosed protecting groups in that the four claimed protecting groups do not have a nitrobenzyl moiety. Instead, they have a nitrophenyl moiety. Another difference between the four claimed protecting groups and many of the nitrobenzyl protecting groups disclosed by the '087 Patent is with respect to substituents. The four claimed groups are unsubstituted nitrophenyl groups. Four of the five nitrobenzyl groups in the '087 Patent are substituted nitrophenyl groups; one (NBOC) is unsubstituted. In the Restriction Requirement, a methoxy-substituted nitrophenyl protecting group was deemed to be patentably distinct from an unsubstituted nitrophenyl protecting group. By this standard, the four claimed protecting groups, all of which have unsubstituted nitrophenyl moieties, are patentably distinct from four of the five disclosed substituted nitrobenzyl groups.

The four claimed protecting groups have additional structural distinctions in comparison to NBOC. The first three protecting groups shown above feature a nitrophenyl moiety directly bonded to an oxycarbonyl or aminocarbonyl moiety, whereas NBOC has a methylene group instead of a direct bond. The fourth protecting group has a thioethylene group connecting the nitrophenyl moiety to the oxycarbonyl moiety. There is no teaching or suggestion in the '087 Patent to modify a nitrobenzylic protecting group to arrive at the recited protecting groups.

Applicant has shown that each of the claimed "nitrobenzylic" protecting groups is structurally and patentably distinct from the protecting groups disclosed in the '087 Patent, and that there is no teaching or suggestion in the cited art of the modification of the disclosed groups to obtain the recited photolabile protecting groups. Moreover, based on the claim groupings

made in the Restriction Requirement for the CIP application and an analysis of the structural features in those groups, the Examiner has deemed the instantly claimed protecting groups to be patentably distinct from many of the protecting groups disclosed in the ‘087 Patent.

### *Conclusion*

Applicant has demonstrated that photolabile protecting groups claimed in the present application are structurally distinct from the protecting groups disclosed by the ‘087 Patent and the ‘348 Publication. In the discussion presented above, Applicant has made the simplifying assumption that if a protecting group is not obvious in view of the cited references, then compounds containing that protecting group and methods of using that protecting group are also not obvious. Applicant does not concede, however, that if a protecting group were obvious or anticipated by the prior art, then compounds containing that protecting group or methods using that protecting group would similarly be anticipated or obvious.

In the Office Action, the Examiner has remarked that some of the claimed protecting groups are “encompassed” by the disclosures of the cited references. It appears that the Examiner has equated a genus encompassing a species with the position that the genus renders all members of the species obvious. However, this position is not supported by the law. Instead, “to establish a *prima facie* case of obviousness in a genus-species chemical composition situation, as in any other 35 U.S.C. 103 case, it is essential that Office personnel find some motivation or suggestion to make the claimed invention in light of the prior art teachings” (MPEP § 2144.08). Applicant maintains that the Examiner has not met this burden.

In particular, only three of the seven protecting groups identified by the examiner as “nitrobenzylic” protecting groups actually contain a nitrobenzyl moiety. Of the three protecting groups with a nitrobenzyl moiety, two of the protecting groups have additional elements between the nitrobenzyl moiety and the cleavable oxycarbonyl or aminocarbonyl moiety. (The protecting groups disclosed by the ‘087 Patent have an oxycarbonyl moiety directly bonded to the nitrobenzyl moiety.) The remaining “nitrobenzylic”protecting group features a second cyclic group fused to two aromatic carbons and the methylene carbon of the nitrobenzyl moiety, which finds no parallel in the cited reference. In no case has the Examiner provided an explanation of how the cited references would motivate one skilled in the art to modify the cited reference and

prepare these specific protecting groups, each of which contains at least one structural feature that is distinct from the prior art teachings. Moreover, the Examiner has not explained how one would arrive at the “nitrobenzylic” protecting groups for protecting groups that do not contain a nitrobenzyl moiety.

The rejection is also not consistent with the Restriction Requirement made in the CIP application of the present application. Many of the protecting groups considered to be patentably distinct in the Restriction Requirement have fewer structural distinctions as compared with the recited protecting groups than the prior art protecting groups upon which the obviousness rejection is based. For example, while the Examiner deemed nitro-substituted naphthalene protecting groups to be patentably distinct by virtue of the nitro group being in a different location on the naphthalene ring, the present obviousness rejection is made over a naphthalene-based protecting group that is optionally substituted with a nitro group. Obviously, there are fewer differences between the patentably distinct protecting groups of the CIP application than between the claimed protecting groups and the protecting groups disclosed in the cited references. Thus, the claimed protecting groups must be patentably distinct over the prior art.

For these reasons, protecting groups discussed above, the claimed compounds that include these protecting groups, and the methods of using these compounds are not obvious over the cited references. Reconsideration and withdrawal of the rejection are respectfully requested.

#### CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If

the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned at (978) 341-0036.

Respectfully submitted,

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